Original Research Article

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A Randomized Double Blind Clinical Study to Compare Dexmedetomidine and Labetalol in Attenuation of Cardiovascular Response to Laryngoscopy and Intubation

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Abstract

Background: The pressure response, which is part of a huge spectrum of stress response, results from the increase in sympathetic and sympathoadrenal activity. This study aims to evaluate the effect of dexmedetomidine and labetalol on cardiovascular response to laryngoscopy and intubation. *Methods:* Seventy ASA physical status I and II patients scheduled for elective surgery under general anesthesia requiring tracheal intubation were randomized into two groups, Group D received intravenous (IV) Dexmedetomidine (1.0µg / kg) diluted to 10 ml with normal saline, infused over 10 mins, 10min prior intubation and group L received IV labetalol 0.3mg/kg diluted to 10ml with normal saline over 2mins, 5min prior intubation. Heart rates (HR), systolic blood pressure (SBP), diastolic blood pressure(DBP) Mean arterial pressure(MAP), rate pressure product (RPP) and adverse effects were recorded at baseline (T0) , 2 min after administration of study drug (T1), 1min after induction (T2) and at 1min (T3), 3min (T4), 5 min (T5) and 10min (T6) after intubation. *Results:* There was a significant fall in HR, MAP and RPP in group D than group L at T1 and T2. After intubation HR (83.20±11.396 vs 94.00±8.898), MAP (87.09±10.942 vs 94.94±10.942) and RPP (9.46±1.777 vs 11.82±1.855) were significantly lower in group D than group L. *Conclusion:* Administration of a single preinduction IV dexmedetomidine at the dose of 1µg/kg resulted in significant attenuation of the rise in the heart rate, systolic blood pressure, diastolic blood pressure, mean blood pressure and rate pressure product than labetalol 0.3mg/kg.

Keywords: Dexmedetomidine; Labetalol; Hemodynamic Response; Intubation; Laryngoscopy.

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Introduction

Laryngoscopy and tracheal intubation may trigger reflex responses causing profound variation in cardiovascular physiology, and may cause serious complications in patients with underlying coronary artery disease, hypertension, or intracranial neuropathology [1]. Various drugs have been used to attenuate these responses, but none have been entirely successful [2]. Dexmedetomidine, the pharmacologically active d-isomer of medetomidine, is a selective α2-adrenoceptor agonist that provides multimodal features like sedation, hypnosis, analgesia and sympatholysis. It also decreases levels of catecholamines during surgery and maintains intraoperative haemodynamics. Various studies have evaluated its hypnotic, analgesic, and anxiolytic properties in the intraoperative period and critical care setting [3-8]. Labetatol is an α1 and non- selective β-adrenergic blocking drug. It is used mainly for perioperative control of blood pressure and

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haemodynamic stability [9]. Hence this study was conducted to compare dexmedetomidine with labetalol to assess the haemodynamic responses to laryngoscopy and intubation under general anaesthesia.

Materials and Methods

After obtaining approval from the institutional ethics committee the study was registered in the Clinical Trial Registry of India as CTRI/2018/02/012012. A written informed consent was taken from each patient who met the inclusion criteria, before enrollment into the study. This was a prospective, randomized, double-blind study. A total of 70 ASA land II patients of either gender between 18 to 65 years of age undergoing elective surgery under general anesthesia requiring endotracheal intubation were included. Patients with known hypersensitivity to study drugs, patients with cardiovascular, respiratory, hepatic or renal diseases, baseline MAP less than 70 mmHg and HR less than 60 beats per minute (bpm), concomitant use of medications which may exaggerate the heart rate response of Dexmedetomidine including digoxin or β-adrenergic antagonists, predicted difficulty in intubation, pregnancy, nursing women and morbidly obese patients were excluded from the study.

A computer-generated randomisation table was generated prior to commencement of study and the allocation concealment was performed using sequentially numbered, coded, sealed envelopes. The study drugs were prepared in identical-looking syringes by an anaesthesiologist who was not involved in the recording of observations. The contents of syringes were unknown to the anesthesiologist involved in the administration of the drug and recording of observations. Decoding was performed on completion of the study. All patients received two syringes labelled A and B, Syringe-Acontents were injected 10 min prior intubation over 10mins and syringe-B contents injected over 2mins, 3min after drug A (i.e., 5min before intubation). For group D: syringe-A was loaded with dexmedetomidine 1mcg/kg diluted to 10ml with NS (normal saline), and syringe-B was loaded with 10ml NS. For group L patients, syringe-A contained 10ml NS and syringe-B was loaded with 0.3mg/kg labetalol diluted to 10 ml with NS.

Patients were premedicated with oral alprazolam 0.25 mg night before surgery and kept fasting for 6 hours prior to surgery. On arrival in the operating room, routine standard monitors such as continuous ECG, NIBP and pulse oximeter were established and the patients' baseline heart rate, blood pressure and oxygen saturation (SpO_2) were recorded after 5 min settling in the operative room. A 20G intravenous cannula was inserted for drug and continuous fluid administration.

All patients were premedicated with intravenous (IV) Glycopyrrolate (0.05mg/kg), IV midazolam (0.03mg/kg), IV Fentanyl (2μg/kg) for analgesia. To maintain double blinding, patients in group D received syringe A which contained IV dexmedetomidine 1.0μg/kg diluted to 10 ml with normal saline, infused over 10 mins, 10mins prior intubation and syringe B which was 10ml normal saline over 2mins, 5min prior intubation and patients in group L received contents of syringe A as 10ml of NS over 10min, 10min prior intubation and contents of syringe B which was 0.3mg/kg labetalol diluted to 10ml with NS over 2min, 5min prior intubation. All patients were induced with IVpropofol 1% till the loss of verbal response.

After ensuring the ability to ventilate, patients were relaxed with IV vecuronium (0.1 mg/kg.). Laryngoscopy was done with appropriate sized Macintosh blade and intubation with appropriate sized cuffed endotracheal tube within 15 seconds at single attempt by the same anaesthesiologist. Ventilator settings were adjusted to maintain $SpO_2 \geq 95\%$ and $ETCO_2$ 30-35mmHg. Anaesthesia was maintained with oxygen, N_2O, isoflurane intermittent positive pressure ventilation and vecuronium. After completion of surgery, anesthesia was discontinued and residual neuromuscular blockade was reversed with IV neostigmine 0.05 mg/kg and IV glycopyrrolate 0.02 mg/kg.

The heart rate through ECG, systolic blood pressure, diastolic blood pressure, mean arterial pressure NIBP in mm/Hg, rate pressure product calculated by formula (SBPX HR/1000) and SpO_2 using pulse oximeter were monitored continuously and recorded at baseline (T0), 2 min after administration of drug(T1), 1min after induction (T2) and at 1 min (T3), 3 min (T4), 5 min (T5) and 10 min (T6) after intubation.

Complications during the study period were recorded and managed accordingly. Hypotension was considered significant when MAP was less than 20% below pre-induction values and was managed by decreasing the delivery of anesthetic agents and IV ephedrine 6 mg increments when needed. Bradycardia (HR <60 bpm), if associated with low MAP or HR <20% pre-induction values, was treated with atropine 0.6 mg. Tachycardia (HR >20% pre-induction values) was managed by increasing the anesthetic depth and treatment of any other possible

cause such as inadequate oxygenation, ventilation or analgesia. Cases were excluded from study if there was more than one attempt at laryngoscopy and intubation and Cormack Lehanne grade >2.

All raw data were subsequently entered into a Microsoft Excel. Data was transferred to statistical package of social sciences (SPSS) version 16. Descriptive statistics was done and presented in tables. To compare dexmedetomidine and labetalol independent sample t test was used. Considering confidence level of 95%, test power of 90% and standard deviation of 1, sample size of 34 per group was required which was rounded to 35 each group considering the drop outs. All data were expressed as mean and standard deviation (95% confidence interval) and $p<0.005$ was considered significant.

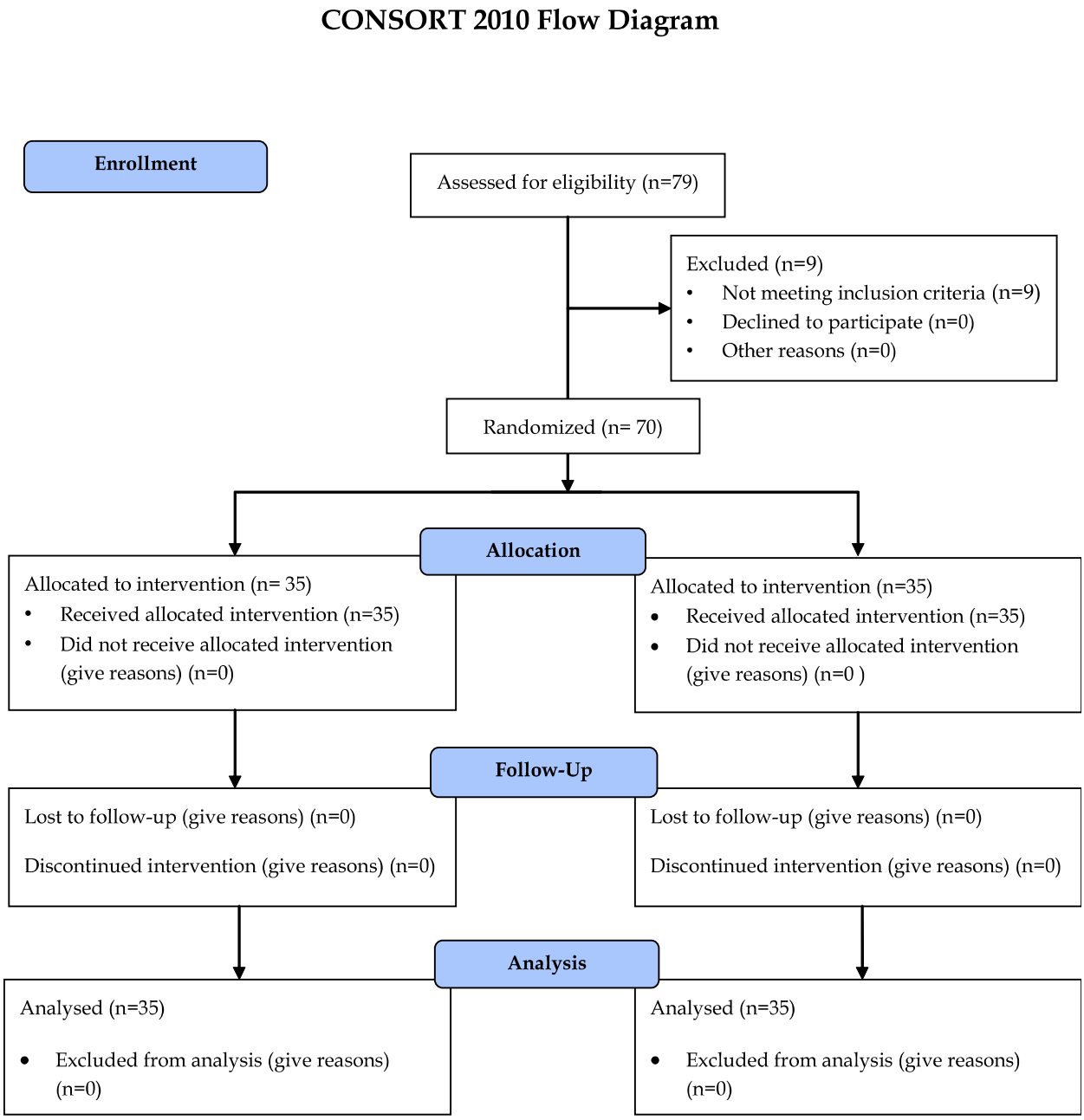

Fig. 1: CONSORT flow diagram of patients included in the study

Results

Figure 1 shows flow diagram for this study where 79 patients were assessed for eligibility and 70 patients wereincluded and their results were analysed.The two groups were comparable in patient characteristics with respect to age, gender, ASA physical status and mean weight (p>0.05) [Table 1]. The baseline hemodynamic parameters were comparable in both the groups.

The heart rate was comparable between both the groups at baseline (T0). Group D showed highly significant(p< 0.000)reduction in HRat T1 than group L (71.74 12.971 vs.88.46±11.173). 1min after intubation the raise in HR was significantly higher in group L (94.00± 8.898) than group D (83.20± 11.396). At T4-T6 there was significant reduction in HR in group D than group L (p<0.05) (Figure 2).

There was a significant reduction in mean SBP, DBP and MAP in group D (106.60±15.25, 70.66±13.35 and 82.60±13.46 respectively) after induction than group

Table 1: Demographic profile of patients

	Group D	Group L	p-value
Age	35.54+10.910	32.74+12.603	0.324
Gender			
Female	23	21	0.627
Male	12	14	
Weight	78.3 ± 12.7	76.5 ± 11.4	0.639

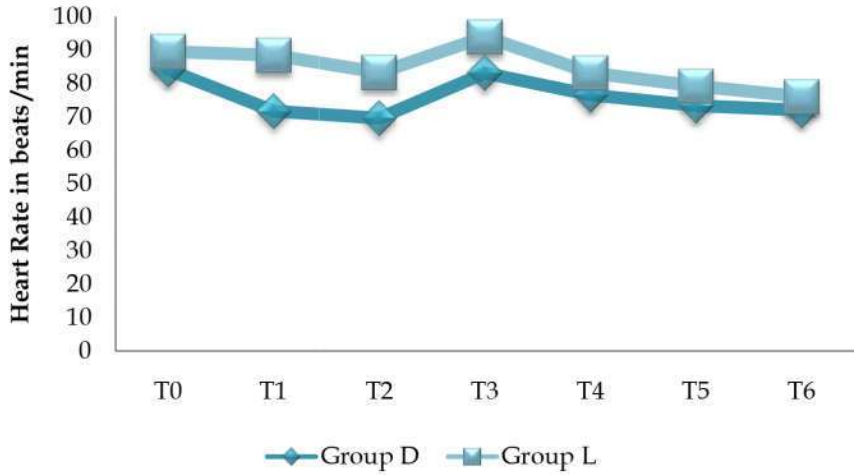

Fig. 2: Comparison of mean HR between Group D and Group L

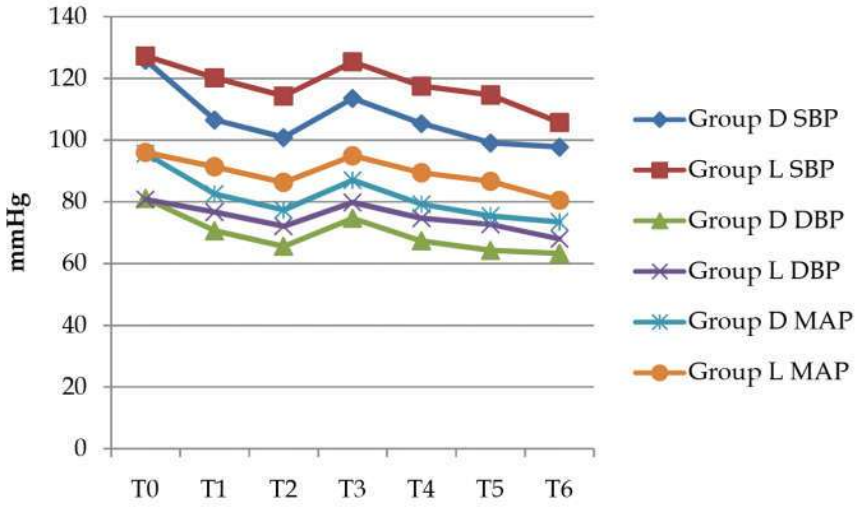

Fig. 3: Comparison of mean SBP, DBP and MAP between Group D and Group L

L (120.26±12.154, 76.74±13.34 and 76.74±13.34 respectively). At 1min after intubation the raise in SBP, DBP and MAP was significantly higher in group L than group D (MAP 87.09±10.942 VS87.09± 10.942) and significantly higher reduction in SBP, DBP and MAP were observed in group D than Group L at T4-T6 (Figure 3).

Figure 4 shows mean rate pressure product (RPP is the product of heart rate and systolic blood pressure/ 1000). The baseline values were comparable in both the groups. After giving study drug, induction, at laryngoscopy and intubation until 10 minutes of intubation mean RPP was significantly low($p<0.000$) in group D than group L.

None of the patients had hypotension or respiratory depression in either group, except onepatient in dexmedetomidine group who had bradycardia which was corrected withIV atropine 0.6mg.

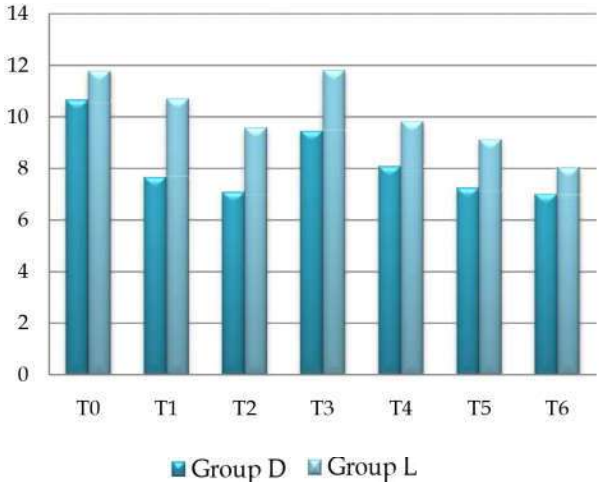

Fig. 4: Comparison of mean RPP between Group D and Group L.

Discussion

The haemodynamic responses to laryngoscopy and endotracheal intubation results in increase in blood pressure and heart rate and hence the rate pressure product (RPP). A high RPP indicates a potential danger of myocardial ischemia. Prophylaxis include topical lignocaine sprays, deeper planes of anesthesia by inhalational agents; narcotics, calcium channel blockers, vasodilators such as sodium nitroprusside; nitroglycerine etc. [2], but they have got side effects such as sedation, respiratory depression, hypotension and bradycardia. Dexmedetomidine has sedative, anxiolytic, analgesic and sympatholytic, effects may blunt the cardiovascular responses in the perioperative period without causing significant respiratory depression [4-8]. Labetelol is unique in that it has the properties of a β adrenergic blocking drug while possessing weak α blocking potential as well [9]. Labetalol was injected 5mins prior intubation in this study as it has a peak effect in 5-15 minutes after administering intravenously and is redistributed very rapidly. It decreases systemic vascular resistance (α1 blockade) and hence decrease in blood pressure whereas the reflex tachycardia which is triggered by vasodilatation is simultaneously blocked by β receptor-blockade. A number of clinical researches have been done stating that dexmedetomidine decreases the haemodynamic responses to laryngoscopy and intubation [4-8] and studies have been done using labetalol in low as well as in higher doses with several anaesthetic regimes for controlling the haemodynamic responses [9-11], but studies are lacking comparing dexmedetomidine 1μg/kg with labetalol 0.3mg/kg for the same purpose. Hence, we compared these two agents for attenuation of stress response during laryngoscopy and intubation.

Scheinin et al. [3] reported that 0.6μg/kg dexmedetomidine decreased, but not totally suppressed, the hemodynamic response to tracheal intubation in healthy individuals. Keniya et al. stated that the pre treatment with dexmedetomidine 1.0 μg/ kg attenuated, but not totally obtunded the cardiovascular response to tracheal intubation after induction of anesthesia [5]. The present study showed greater fall in hemodynamic parameter as compared to keniya et al probably because we used 2mcg/kg fentanyl and propofol induction in contrast to fentanyl 1mcg/kg and thiopentone induction by keniya et al. Our study showed Fall in HR and MAP between 13-19% in contrast to 10-15% in astudy conducted by Bajwa et al, this difference is due to lower dose of dexmedetomidine used by Bajwa et al. (0.5mcg/kg dexmedetomidine) [5]. Jaakola and colleagues noted that after insertion of endotracheal tube the maximum heart rate was 18% less ($p=0.036$) in group D compared to placebo group. Within 10 min after intubation maximum systolic and diastolic pressures were also significantly ($p=0.013$ and $p=0.020$) lesser in dexmedetomidine group [6].

Although labetalol had maintained the blood pressure, tachycardia was still prominent during laryngoscopy and intubation. It had partial effect to maintain the rise in heart rate. Singh et al. [9] compared labetalol in the dose of 0.25mg/kg with esmolol and found labetalol to be superior in attenuation of pressor response. Ramanathan et al. [10] used 20 mg labetalol to prevent rise in SBP successfully in pre-eclamptic patients. Inada et al. [11] found 10 mg (0.14 mg/kg) labetalolwas

noteffective in attenuating the rise in systolic pressure. This was probably due to the lower dose they used and the timing of administration of labetalol (2 min prior to intubation) because of which the peak effect of drug was lost at intubation.

Dexmedetomidine causes bradycardia due to central sympatholysis and resultant unopposed vagal tone and possibly due to presynaptic mediated diminution of noradrenaline release. In our study the incidence of bradycardia was found to be 3%.

Conclusion

This Study concludes that a single dose of dexmedetomidine 1μg/kg given over 10mins prior to induction of anesthesia significantly attenuated the hemodynamic response associated with laryngoscopy and intubation when compared to single dose of labetalol 0.3mg/kg. Labetalol did not attenuate the tachycardia during laryngoscopy and intubation.

Conflict of Interest: None

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